

# The Effect of COVID 19 on Liver Parenchyma Detected and measured by CT scan Hounsfield Units

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**Background:** COVID 19 may affect organs other than lungs, including liver, leading to parenchymal changes. These changes are best assessed by unenhanced computed tomography (CT). We aim to investigate the effect of COVID 19 on liver parenchyma by measuring the attenuation in CT scan Hounsfield unit (HU). **Materials and Methods:** A cohort of patients, who tested COVID 19 polymerase chain reaction positive, were enrolled and divided into two groups: fatty liver (FL) group (HU ≤ 40) and nonfatty liver (NFL) group (HU > 40) according to liver parenchyma attenuation measurements by high resolution noncontrast CT scan. The CT scan was performed on admission and on follow up (10–14 days later). Liver enzyme tests were submitted on admission and follow up. **Results:** Three hundred and two patients were enrolled. Liver HU increased significantly from 48.9 on admission to 53.4 on follow up CT scan (P<0.001) in all patients. This increase was more significant in the FL group (increased from 31.9 to 42.9 [P =0.018]) Liver enzymes were abnormal in 22.6% of the full cohort. However, there was no significant change in liver enzymes between the admission and follow up in both groups. **Conclusion:** The use of unenhanced CT scan for assessment of liver parenchymal represents an objective and noninvasive method. The significant changes in parenchymal HU are not always accompanied by significant changes in liver enzymes. Increased HU values caused by COVID 19 may be due to either a decrease in the fat or an increase in the fibrosis in the liver.

**Key words:** Computed tomography scan, COVID-19, fatty liver, hepatic steatosis, Hounsfield unit, liver enzymes, liver fibrosis, liver parenchyma injury

**How to cite this article:** Fataftah J, Tayyem R, Qandeel H, Baydoun HA, Al Manasra AR, Tahboub A, *et al.* The effect of COVID 19 on liver parenchyma detected and measured by CT scan hounsfield units. J Res Med Sci 2022;27:26.

## INTRODUCTION

COVID-19 tends to target the respiratory tract, causing anywhere from mild to severe illnesses and pneumonia. Recently, there has been evidence that COVID-19 can affect other organs, with more than half of COVID-19 patients showing varying degrees of liver disease and injury.<sup>[1-4]</sup> The liver injury secondary to COVID-19 usually manifests as mild transient elevation of transaminases and, to a lesser extent, elevation in bilirubin, alkaline phosphatase, and

gamma-glutamyltransferase. The exact mechanism is not well understood.<sup>[4]</sup> Infections with other coronavirus strains, i.e. severe acute respiratory syndrome coronavirus 1 and the Middle East respiratory syndrome coronavirus, have also been linked to hepatic insult.<sup>[5,6]</sup>

Fatty liver (FL) is a common disease, with a prevalence of 20%–30% in the adult population and 70% in diabetic patients.<sup>[7]</sup> It is normal for the liver in healthy individuals to contain some fat, but a fat content more than 5% of the liver mass is classified as steatosis.<sup>[8]</sup> Fat deposition in the liver can lead to liver inflammation, scarring, and

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10.4103/jrms.JRMS\_1228\_20

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**Submitted:** 18-Nov-2020; **Revised:** 28-Mar-2021; **Accepted:** : 23 June 2021; **Published:** 17-Mar-2022

finally, cirrhosis with liver failure.<sup>[9]</sup> Among FL patients who develop steatohepatitis, half evolve into fibrosis, 10%–15% to cirrhosis, and 5.4% to hepatic insufficiency.<sup>[7,10]</sup>

Different morphological traits are utilized in unenhanced computed tomography (CT) for diagnoses of liver steatosis and cirrhosis. These traits rely on visual recognition of organ changes such as size and shape of the liver, contrast changes, and apparent image radiopacity.<sup>[11]</sup> The attenuation of CT scan X-ray beam depends on the thickness of the organ traversed and the composition, mainly the tissue density in the path of the X-ray beam.<sup>[12]</sup>

Hounsfield unit (HU) is utilized in CT scanning to express numbers in a standardized and convenient form. HU is obtained by measuring the linear attenuation coefficients. The attenuation values are expressed on an arbitrary scale, with water density being 0 HU and bone density being 1000 HUs. The liver parenchyma is normally homogeneous; typically, the liver's attenuation is 50–60 HUs. In FL, the tissue density will be less due to greater fat content. Therefore, liver density (attenuation in HU) is inversely correlated to liver fat content.<sup>[7]</sup> Liver HU on unenhanced CT provides a simple, fast, objective, and noninvasive way to assess liver fat content.<sup>[12]</sup> Various studies reported the use of a single absolute value of 40 HU or less on unenhanced CT as a good method to diagnose moderate-to-severe FL disease.<sup>[13,14]</sup>

This study aims to investigate the effect of COVID-19 illness on liver parenchyma by measuring the attenuation in CT scan HU and to understand the possible mechanism for these alterations. Early recognition of hepatic insult due to COVID-19 virus may help physicians to alter treatment protocol and to consider discontinuing any medications that might worsen the hepatic injury.

## MATERIALS AND METHODS

This is a retrospective study conducted at Prince Hamzah Hospital, Amman, Jordan. All adult patients diagnosed with COVID-19 by polymerase chain reaction and admitted to our center during the period from March to June 2020 were included in the study. Demographic, clinical, and laboratory data were collected. A Philips Brilliance 16 CT Scanner was used to undertake chest CT scans of all patients with the same settings. The dose protocol used in this study consisted of 120 kVp and 25–75 mAs.

High-resolution noncontrast CT scan of the chest was carried out for those patients on arrival as part of their admission protocol. The upper abdomen was included by default in every CT scan of the chest. All the images were interpreted by a single radiologist with more than 10-years' experience in diagnostic radiology. Homogeneous areas in

the liver CT scan were sampled to represent the parenchyma, with avoidance of vessels, focal lesions, bile ducts, focal changes of FL or fatty sparing, and surface margins. Liver HU was measured and recorded for each patient. Follow-up noncontrast CT scan was repeated 10–14 days after admission as part of patient management protocol for patients with abnormal CT scan findings on admission.

This study was approved by our university research ethics and development committee IRB ref. number:2000353 (No. 9/3/2020/2021).

Statistical analysis was performed using the Statistical Package for the Social Scientists version 17. (1 New Orchard Road, Armonk, New York 10504-1722, United States). Paired samples *t*-test was used to compare continuous scores of the same group on two occasions (admission and follow-up). Pearson's Chi-squared test was used to assess categorical data sets. Data difference was considered to be statistically significant when its  $P \leq 0.05$ .

## RESULTS

Three hundred and two patients were included in this study. Their mean age was 31.5 years (standard deviation [SD]=19.3) and their mean body mass index was 24.9 (SD = 7.7). One hundred and sixty-seven (55.3) patients were male. Twelve (4%) patients were admitted to intensive care unit and nine (3%) of them died. Patients were divided into two groups according to their HU reading on admission: FL group (14% of the cohort) with HU  $\leq 40$  and nonfatty liver (NFL) group (86% of the cohort) with HU  $>40$ .

Liver HU significantly increased in both the FL and NFL groups [Table 1]. Liver enzymes were abnormal in 22.6% of the total cohort. However, there was no statistically significant difference between the two groups on admission [Table 2]. The liver enzymes were not statistically significantly different between the two groups on follow-up measurement [Table 2].

## DISCUSSION

The significant increase in the HU in the FL group could be explained by either liver parenchymal injury in the form of fibrosis or by decreased fat in the liver and consequently resolution of liver steatosis. The significant change in HU is not specific to the FL group. Many patients in the NFL group scored HU values within normal range (40–60) at admission, however, they deviated significantly from their baseline HU after 10–14 days of COVID-19 disease treatment course. The alteration in density of liver texture in the NFL group may also be attributed to fibrosis or to decreased liver fat and regression of steatosis level.

**Table 1: Paired samples t-test on liver Hounsfield unit on admission and on follow-up**

	Mean (SD)	t	Df	Significant (two-tailed)
Liver HU on admission/all	48.9 (11.1)	-4.2	54	<0.001
Liver HU on follow-up/all	53.4 (9.1)			
Liver HU on admission/HU ≤40 (FL group)	31.9 (7.8)	-6.0	10	<0.001
Liver HU on follow-up/HU ≤40 (FL group)	42.9 (10.7)			
Liver HU on admission/HU >40 (NFL group)	53.2 (6.9)	-2.5	43	0.018
Liver HU on follow-up/HU >40 (NFL group)	56.0 (6.5)			
Independent samples t-test to compare difference in mortality between liver HU >40 and liver HU ≤40				
Mortality among patients with liver HU >40 (NFL group)	4.5 (0.7)	1.9	1.2	0.2
Mortality among patients with liver HU ≤40 (FL group)	7.5 (1.2)			

SD=Standard deviation; HU=Hounsfield unit; FL=Fatty liver; NFL=Nonfatty liver

**Table 2: Comparison of liver enzymes between patients with fatty liver and nonfatty liver**

	Mean (SD)		P
	HU ≤40 (FL group)	HU >40 (NFL group)	
Levels measured on admission			
ALT	30.6 (20.1)	22.5 (14.5)	0.104
AST	29.7 (11.5)	24.1 (10.8)	0.124
Levels measured on follow-up			
ALT	28.3 (16.0)	23.1 (13.2)	0.114
AST	26.8 (10.8)	23.5 (10.3)	0.098

SD=Standard deviation; HU=Hounsfield unit; ALT=Alanine aminotransferase; AST=Aspartate aminotransferase; FL=Fatty liver; NFL=Nonfatty liver

With regard to the liver injury and fibrosis, the literature indicates a direct effect of COVID-19 virus leading to hepatocellular injury (hepatitis) by hepatocyte and bile duct cell expression of angiotensin-converting enzyme 2 (ACE2) receptor, which is a target receptor for COVID-19. COVID-19 binds ACE2 on cholangiocytes which may lead to cholangiocyte dysfunction and inducing systemic inflammatory process leading to liver injury.<sup>[2]</sup> Because its expression is higher in bile duct cells, they are more likely to be affected by COVID-19 infection.<sup>[15]</sup>

With regard to the other possibility of decreased liver fat and consequently resolution or regression of liver steatosis, this could be explained by the healthier diet provided to the patients during their 2 weeks of admission. However, multiple factors are enrolled in the potential pathogenesis of liver injury secondary to COVID-19. Negative balance metabolism and increased catabolism may be mediated by systemic inflammatory responses (cytokine release or storm of the COVID-19 syndrome). Another possible mechanism is drug-related toxicity (primarily antiviral and antimalarial medications).<sup>[2,4,16,17]</sup> Medeiros *et al.* found a significantly higher prevalence of hepatic steatosis among COVID-19-positive individuals. However, the paper concluded that further studies are required to assess the relationships of hepatic steatosis with disease severity.<sup>[18]</sup>

Previous studies showed that abnormal liver function is a common finding in COVID-19 illness (37.2%–60%).<sup>[15,6]</sup> Liver enzymes were abnormal in about a quarter of all

of our patients, and no significant change was noticed in liver enzymes during the hospital stay in either the FL or the NFL group. This may indicate that the alteration in the liver parenchyma measured by HU is probably not due to liver injury/fibrosis. Furthermore, Wu *et al.* did not find a correlation between liver enzymes, total bilirubin, alkaline phosphatase, albumin and other liver function indicators, and severe COVID-19.<sup>[4]</sup> Liver damage in patients with mild COVID-19 is usually temporary and can get back to normal without any special treatment.<sup>[4,19]</sup>

Further research is required to fully understand the underlying mechanisms leading to alteration of liver parenchyma during COVID-19 illness. Future research could look at the histological examination of the liver compared to the CT scan measurements.

## CONCLUSION

The use of unenhanced CT for assessment of liver attenuation represents an objective and noninvasive method for detection of asymptomatic liver parenchymal changes. The significant changes in parenchymal HU may not be accompanied by significant changes in liver enzymes. Increased HU values caused by COVID-19 may be due to either a decrease in the fat or an increase in the fibrosis in the liver.

## Financial support and sponsorship

Nil.

**Conflicts of interest**

There are no conflicts of interest.

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